

AMENDMENTS TO THE DRAWINGS:

A replacement drawing is submitted for Figure 22. The legend "PRIOR ART" has been added.

REMARKS

The application has been amended to place the application in condition for allowance at the time of the next Official Action.

A substitute Abstract of the Disclosure is submitted taking into account the suggestions noted in the Official Action. By the above, the objection to the abstract is believed addressed and withdrawal of the same is respectfully requested.

The specification is amended including incorporating the suggestions noted on page 3 of the Official Action to address idiomatic and grammatical errors. The changes to the specification do not present new matter and are believed to address the specification objection noted in the Official Action.

A replacement drawing is submitted for Figure 22 labeling this figure as "PRIOR ART" as disclosed on page 19, line 27 through page 20, line 1 of the application as filed. The above change is the only change and is believed not to introduce new matter.

Claims 1-8, 10-12, 16, 17, 21-26, 30, 31, 34 and 35 were previously pending in the application. Claims 8 and 17 are canceled and new claims 36-39 are added. Therefore, claims 1-7, 10-12, 16, 21-26, 30, 31 and 34-39 are presented for consideration.

Applicants note with appreciation the indication that claims 6, 7, 11 and 12 are allowable.

Claims 5, 8, 21, 22 and 34 were rejected under 35 USC 103(a) over CARLE et al. 5,167,790 in view of CHAN et al. 6,696,022. That rejection is respectfully traversed.

Claim 5 is amended and recites a channel through which a sample containing components-to-be-separated moves. The channel has a plurality of compartments partitioned by one, or two or more bent portions of the channel. Claim 5 further recites an external force imposing unit imposing a plurality of external force imposing patterns having different imposing directions from each other to the components-to-be-separated so as to allow them to move through the channel.

Using the above recited features, a specific component can be separated in a specific compartment. Further, even when an additional sample is introduced after the separation of the previously added sample is completed, the newly added sample can be separated as well with the previously added sample to obtain concentrated components.

CARLE discloses a method and apparatus for gel electrophoresis which employs periodic inversion of the electric field essentially in one dimension, denoted as FIGE, results in net migration by using a longer time or higher voltage in one direction than in the opposite direction. FIGE permits separation of DNA or protein mixtures in size ranges not accessible to ordinary electrophoresis (as described in abstract).

It is disclosed in Col. 4, pages 14-24 of CARLE that "the successful results achieved with the field-inversion gel electrophoresis system of this invention were surprising and unexpected" and "They were also not predicable from existing molecular theories of electrophoresis".

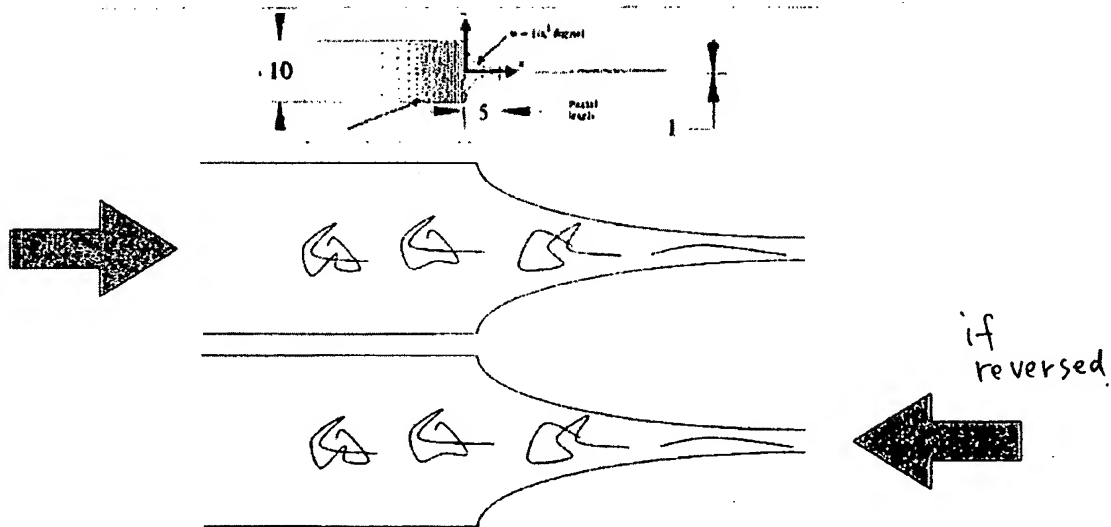
In CHAN, polymers are loaded into a device and run through the structure. Stretching is achieved by applying shear forces as the polymer passes through the structures, placing obstacles in the path of the polymer, or a combination thereof. Since multiple molecules may be stretched in succession, extremely high throughput screening is achieved. The object of CHAN is to stretch the molecules. For this object, the structure of CHAN has such that prealignment, contracting flow, or elongation flow easily occurs.

As the object of CHAN is to stretch the molecules, if the reverse direction of the external force is imposed, the stretched molecules become original circle structure and thus the object of CHAN cannot be obtained.

For example, as shown in Fig. 1 of CHAN, in elongation flow, the tapered structure is essential. However, the tapered structure is not symmetrical in the flow direction. This means that if the flow is reversed, the effect for stretching the molecules functions in reverse. Therefore, the stretched structure becomes the original circle structure (See explanatory Fig. 1 below).

As CHAN increases the throughput by stretching, by applying reverse flow, the throughput is lowered.

Explanatory Fig. 1



The structure of CHAN is provided in order to stretch the molecule. CHAN does not disclose moving the samples in the reverse direction. Nevertheless, as set forth above, if the samples are moved in reverse, the high throughput that CHAN desires cannot be obtained. Thus, the proposed combination would not be desirable and therefore, one of ordinary skill in the art would not be motivated to make the proposed modification.

In addition, even if one were motivated to make the proposed modification, the references do not disclose all that is recited.

Page 5, line 1 to page 6, line 5 of the Official Action indicates that CARLE discloses "Compartments". However, the "compartments" of CARLE are bands formed as a result of electrophoresis and usually noted as "demarcation" or the like and are clearly different from the compartment of the present invention. Further, the lanes A, B, C, D, E of CARLE are totally different from the compartment of the present invention and rather "a lane" corresponds to "a channel" as different samples are introduced into the lanes A, B, C, D, E as described in column 11, lines 15-28 in CARLE. CHAN does not disclose compartments.

The above-noted feature is absent from each of the references, is absent from the combination, and thus, would not have been obvious to one having ordinary skill in the art.

Independent claim 21 includes similar features and the analysis above regarding claim 5 is equally applicable to claim 21.

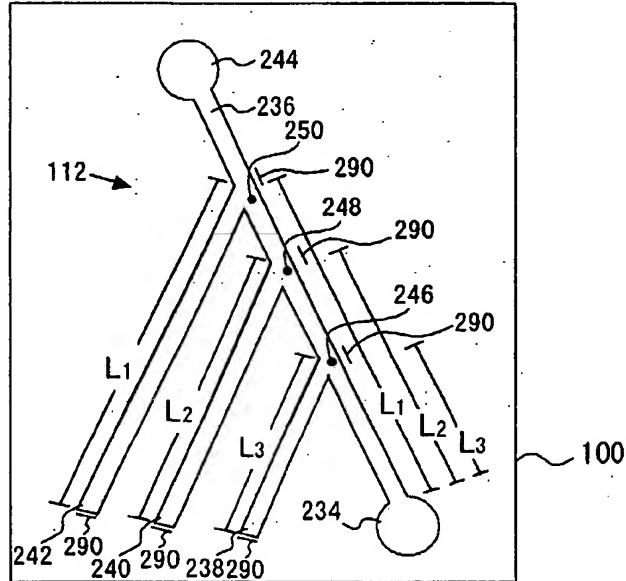
Claims 16, 17, 30 and 31 were rejected under 35 USC §103(a) as being unpatentable over CARLE et al. in view of CHAN et al. and further in view of SHIMOIDA et al. 7,105,354. That rejection is respectfully traversed.

Independent claim 16 is amended and recites that a channel has a main channel and sub channels formed as being branched out from the main channel, through which a sample including components-to-be-separated moves. The main channel has

one end where a sample introduction port is provided and the other end placed downstream of the one end. Claim 16 further recite an external force imposing unit imposing a plurality of external force imposing patterns having different imposing directions from each other to the components-to-be-separated so as to allow them to move through the channel.

By way of example, as seen in Figure 11 of the present application, reproduced below, main channel 236 has sub channels 238, 240 and 242 branching out therefrom. Each of the sub channels 238, 240 and 242 include an external force imposing unit 290 at a distal end thereof. See also page 45, lines 2-5.

FIG. 11



The Official Action recognizes that CARLE et al. as modified by CHAN et al. do not show a channel having a main channel and sub channels. The Official Action offers SHIMOIDA as expressly reciting a main channel having a plurality of sub channels. In any event, as set forth above, the combination of CARLE and CAHN is improper. The addition of SHIMOIDA does not overcome this shortcoming

Moreover, none of the references disclose that which is recited. Specifically, none of the above-noted embodiments of Figure 1 of CHAN disclose an external force imposing unit imposing a plurality of external force imposing patterns having different imposing directions from each other to the components-to-be-separated so as to allow them to move through the channel. Column 6, lines 38-40 of SHIMOIDA disclose that diversion can be achieved by making one channel branching into multiple channels (diverting a channel). The embodiments of Figures 5-9 of SHIMOIDA disclose sub channels converging with a main channel but do not show an external force imposing unit imposing a plurality of external force imposing patterns having different imposing directions from each other to the components-to-be-separated so as to allow them to move through the channel. Moreover, none of the other embodiments of SHIMOIDA disclose or suggest such feature.

The above-noted feature is missing from each of the references, is absent from the combination, and thus would not have been obvious to one having ordinary skill in the art.

Claims 17, 30, and 31 depend from claim 16 and further define the invention and are believed patentable over the cited combination of references at least for depending from an allowable independent claim.

Claim 10 was rejected under 35 USC §103(a) as being unpatentable over CARLE et al. in view of CHAN et al. and further in view of EBERSOLE et al. 5,578,460. That rejection is respectfully traversed.

Claim 10 depends from claim 5 and is believed to define over the art at least for depending from an allowable independent claim.

Claims 1-4 and 23-26 were rejected under 35 USC §103(a) as being unpatentable over CARLE et al. in view of CHAN et al. and further in view of ANDERSON et al. US Publication No. 2001/0036672 and further in view of PETHIG et al. WO 97/34689. That rejection is respectfully traversed.

Claim 1 recites that an external force imposing unit has a function of alternately executing a first external force imposing pattern by which the external force is imposed to said components-to-be-separated in the forward direction along said channel, and a second external force imposing pattern by which the external force is imposed to said components-to-be-separated

in the direction opposite to the forward direction along said channel, to thereby fractionate said components-to-be-separated into any of said compartments.

As set forth above, CARLE in view of CHAN do not disclose this feature, and moreover, would not have been combined in the manner suggested. ANDERSON et al. and PETHIG et al. are offered for this feature.

However, the references neither provide the motivation to make the proposed modification nor disclose that which is recited.

Section [0133] of ANDERSON is offered for the disclosure of a check valve. Such a check valve is used in the embodiment of Figure 6A of ANDERSON, reproduced below. As disclosed in this section, the embodiment of Figure 6A includes chambers of different pressures. In order to prevent backflow from a previous or subsequent reaction chamber that is at a higher pressure, ANDERSON uses one-way check valves in the fluid channels 644 between the reaction chambers 612, 614, 616.

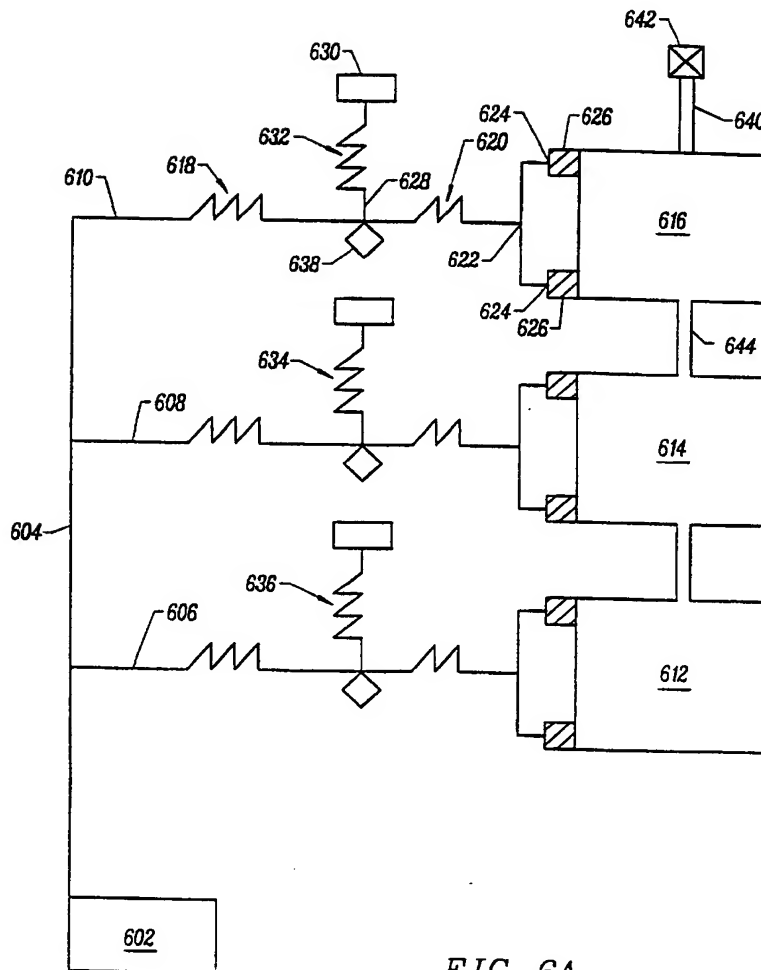


FIG. 6A

Thus, in ANDERSON, check valves are used to prevent backflow when a previous or subsequent reaction chamber is at a higher pressure. As the device of CARLE is not intended to operate with compartments having varying pressures, it would not have been obvious to look to the teachings of ANDERSON for a check valve to prevent backflow based on such chambers having different pressures. Thus, one of ordinary skill in the art would not have been motivated to make the proposed modification.

PETHIG is only cited for the disclosure of a fluid medium that does not flow through the channels. PETHIG does not disclose that which is recited.

The above-noted features are missing from each of the references, are absent from the combination, and thus would not have been obvious to one having ordinary skill in the art.

Claims 4 and 23-26 depend from claim 1 and further define the invention and are believed patentable over the proposed combination of references at least for depending from an allowable independent claim.

Claim 35 was rejected over CARLE et al. in view of CHAN et al., ANDERSON et al. and PETHIG et al. in further view of HANCOCK et al. 5,716,825. That rejection is respectfully traversed.

HANCOCK et al. is only cited for the disclosure of a mass spectrometry system. HANCOCK et al. does not overcome the shortcomings of CARLE et al., CHAN et al., ANDERSON et al., and PETHIG et al. as set forth above with respect to claim 1. Since claim 35 depends from claim 1 and further defines the invention, claim 35 is believed patentable at least for depending from an allowable independent claim.

New claims 36-39 are added. Support for the new claims can be found in the original claims and on page 2, lines 22-26. The new claims are believed patentable at least for depending from an allowable independent claim.

By way of further explanation, according to the present invention, a specific component can be obtained at a specific compartment.

The mechanism in which the components can be desirably separated even when the forward moving period and the reverse moving period are same will be explained.

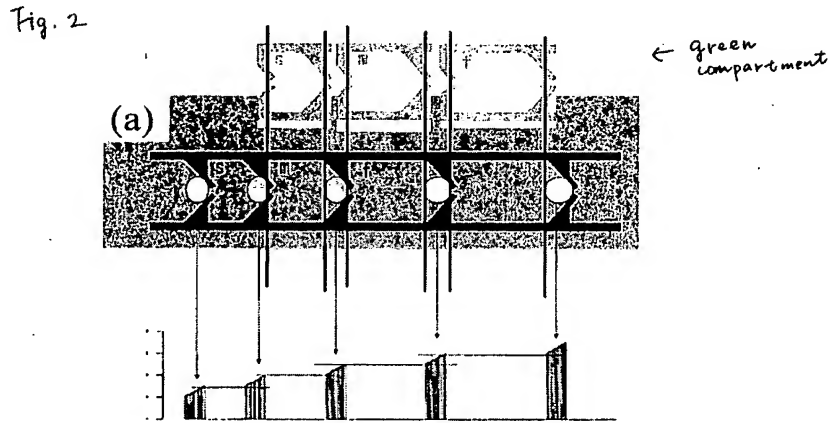
Here, the both moving periods are set as " t ". When the moving speed of the sample is " r ", and the sample is moved forwardly, a DNA fragment moves as long as $(t \times r)$. When the length of the compartment is equal to or larger than $(t \times r)$, the fragment can reach near the exit of the compartment but cannot go into the next compartment. However, when the length of the compartment is shorter than $(t \times r)$, the fragment can pass through the valve and move into the next compartment.

When, on the other hand, the samples are moved in reverse, the fragments in each of the compartments go back to the entrance of a respective compartment and are blocked by the valve and therefore remain in the original compartment.

In explanatory Fig. 2(a), the green compartments express the downstream compartment of each of the black compartments. In this example, the length of the compartment become longer as it goes more downstream. In the compartment expressed as " m ", which is longer than the compartment expressed as " s ", DNA fragments which can move more than the length of the compartment " s " within time " t " and which cannot move more than

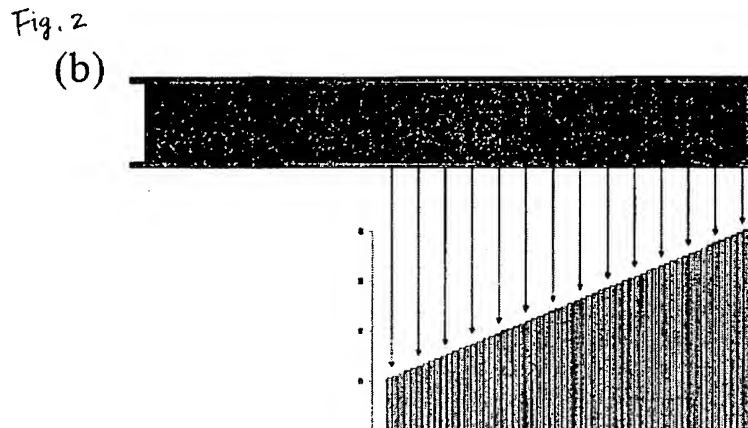
the length of the compartment "m" within the time "t" are trapped.

Explanatory Figure 2(a)



By repeating the forward movement and the reverse movement, the fragments are separated into one of the compartment based on their moving speed characteristics. Thus, the distribution of the moving speed characteristics of the fragments becomes as shown in Fig. 2(a). Explanatory Fig. 2(b) shows the distribution of the moving speed characteristics of the fragments without the mechanism of the present invention.

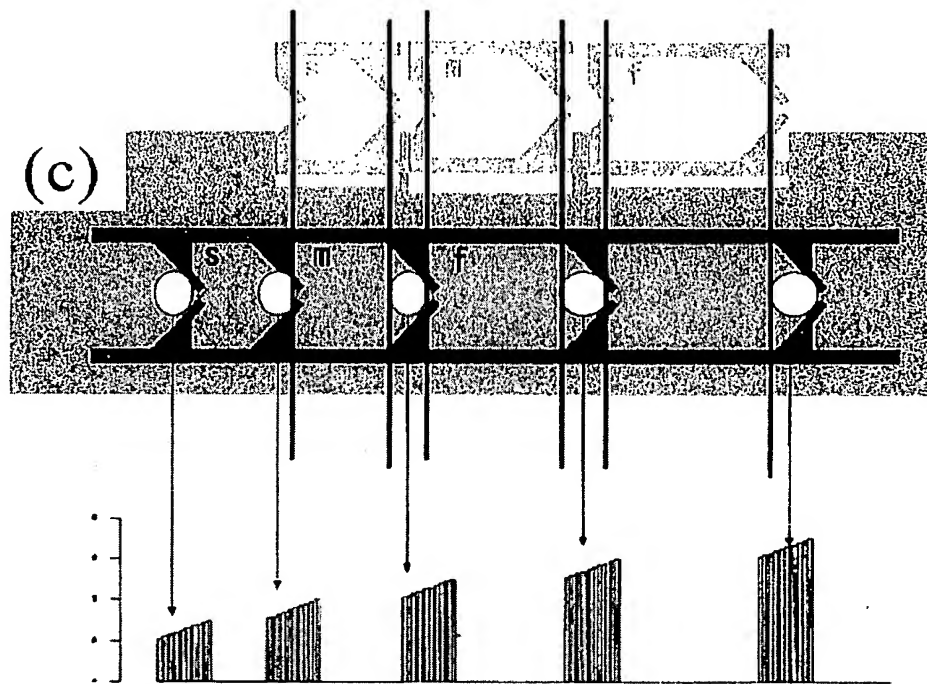
Explanatory Figure 2(b)



According to the present invention, even when the sample is added after the previous sample is already separated as shown in Fig. 2(a), by repeating the above forward and reverse operation, the added sample can be separated as same as the previous separated sample as shown in Fig. 2(c). Here, the amount of the fragments included in each of the compartment is increased.

Explanatory Figure 2(c)

Fig. 2

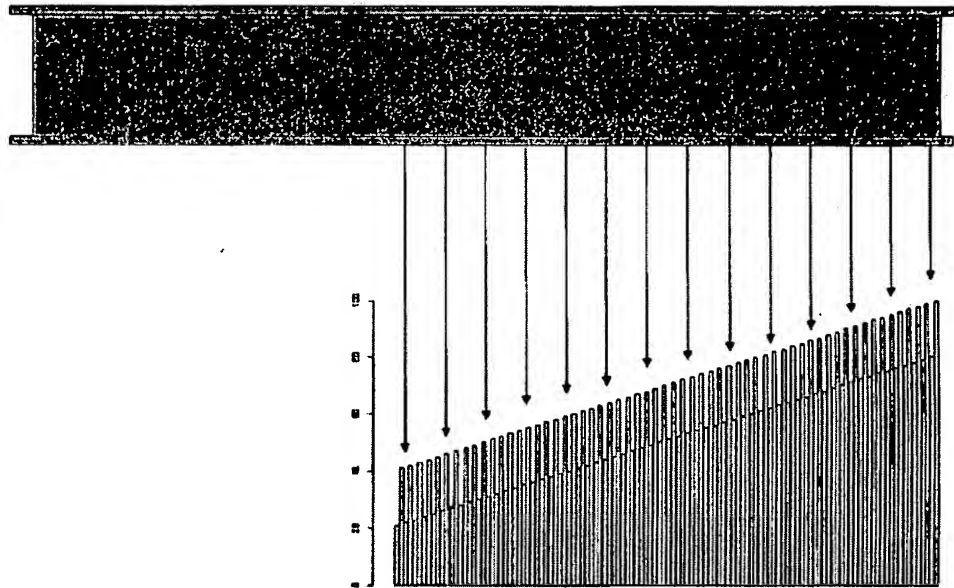


However, by the conventional technique such as disclosed in CARLE or CHAN, while some sample (first sample) is being separate by performing a first electrophoresis and then some sample (second sample) is added in a sample introduction port, and the electrophoresis is continued, the first sample moves further downstream while the second sample is moving.

Thus, fragments having a rapid moving speed in the second sample overlap the fragments having a slow moving speed in the first sample and the samples cannot be separated (as shown in Fig. 2(d)).

Fig. 2

(d)



Thus, the recited forward movement and the reverse movement separate the fragments into one of the compartments in a manner that would not have been obvious in view of the proposed combination of references.

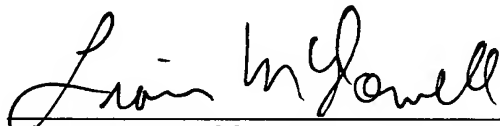
In view of the present amendment and the foregoing remarks, it is believed that the present application has been placed in condition for allowance. Reconsideration and allowance are respectfully requested.

Please charge the fee of \$100 for the two extra claims
of any type added herewith, to Deposit Account No. 25-0120.

The Commissioner is hereby authorized in this,
concurrent, and future replies, to charge payment or credit any
overpayment to Deposit Account No. 25-0120 for any additional
fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following items:

- an amended Abstract of the Disclosure
- a Replacement Sheet for Figure 22 of the drawings